Clinical Edit Criteria Document

Drug/Drug Class: **Epoetin / Darbepoetin**
Implementation Date: **August 4, 2004**
Prepared for: **Missouri Medicaid**
Prepared by: **Heritage Information Systems, Inc.**

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	Ensure patients with prescriptions for epoetin or darbepoetin have appropriate indications for use.
Why was this Issue Selected:	For the previous reporting period of August 2002 to July 2003, Missouri Medicaid paid $7.9 million for epoetin and darbepoetin. This represents 0.8% of the total drug budget.

Program-specific information:

Volume Estimates (per month)	Claims	Patients	Expense
Entire drug class	*2,300*	*674*	*$662,000*
Erythropoetin	*2,220*	*630*	*$615,000*
Darbepoetin	*53*	*44*	*47,000*

Setting & Population: All individuals receiving epoetin or darbepoetin.

Type of Criteria:

☒ Increased risk of ADE ☐ Non-Preferred Agent
☒ Appropriate Indications ☐ Other:

Data Sources: ☐ Only administrative databases ☐ Databases + Prescriber-supplied

Purpose of Clinical Edit

Under the Omnibus Budget Reconciliation Act of 1993, Congress intended Prior Authorization or Prior Approval (PA) programs to control utilization of products that have very narrow indications or high abuse potential. While prescription expenditures are increasing at double-digit rates, payors are also evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. Clinical Edit criteria, which is different from prior authorization or prior approval programs, assist in the achievement of qualitative and economic goals related to health care resource utilization without placing the entire utilization of a drug in a PA status. Screening the use of certain medications on the basis of clinical appropriateness can reduce costs by requiring evidence of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class. Clinical Edit criteria can also reduce the risk for adverse events associated with medications by identifying patients at increased risk due to diseases or medical conditions, or those in need of dosing modifications.

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Why has this clinical Issue been selected for review?

Erythropoietin is a glycoprotein produced by the kidneys that stimulates the formation of red blood cells (erythropoiesis). A recombinant human erythropoietin, epoetin alfa, is available from two different manufacturers (Epogen®, Procrit®). Epoetin alfa has FDA approved indications for the treatment of anemia associated with several conditions: chronic renal failure (with and without dialysis), zidovudine treatment in HIV infected patients, and chemotherapy for non-myeloid cancers. It is also indicated for use prior to elective, noncardiac, nonvascular surgery in order to reduce the need for allogeneic blood transfusions.[1,2] Studies have shown epoetin alfa to improve hematologic indices, reduce the need for transfusions, and improve patient quality of life. Illicit use of epoetin alfa has been reported in athletes wishing to increase their endurance.[3]

Darbepoetin alfa (Aransep™) is the second erythropoiesis-stimulating agent available on the market and is approved for the treatment of anemia associated with both chronic renal failure (with and without dialysis) and chemotherapy for non-myeloid malignancies.[4] It differs from epoetin alfa by containing two additional N-glycosylation sites which serve to lengthen the duration of action of the drug, thereby reducing the dosing frequency required with epoetin alfa. Epoetin alfa is generally dosed several times weekly, while darbepoetin alfa is usually administered once weekly. Both drugs must be administered by IV or SC injection. Additionally, epoetin alfa has been studied and is approved for use in pediatric patients greater than 1 month old, while the safety and efficacy of darbepoetin alfa in pediatric patients has not been established.

Dosing of these agents is highly variable based on the medical condition and needs of the specific patient. Dosing adjustments are made in an attempt to attain target

hematocrit and hemoglobin levels. Suggested hematocrit target range for epoetin alfa is 30%-36%,[1,2] while it is recommended that the darbepoetin alfa dose be titrated not to exceed a hemoglobin of 12 g/dL.[4] Increases in these parameters can take anywhere from 2-6 weeks after a dosing adjustment is made. A number of etiologies may result in a diminished or delayed response. These include iron deficiency; underlying infectious, inflammatory or malignant disease; occult blood loss; underlying hematologic diseases; folic acid or vitamin B12 deficiencies; hemolysis; aluminum intoxication; and osteitis fibrosa cystica. Prior to initiation of therapy and during maintenance therapy, laboratory monitoring, and treatment with iron if necessary, should be conducted to ensure adequate iron stores (transferrin saturation ≥20%, ferritin ≥100 ng/mL).

Cost is a significant factor with use of these agents. It is estimated that for 12 weeks of therapy, a patient requiring 11,000-17,999 units/week of Procrit® would need about 40 mcg/week of Aranesp™, with associated costs of $1,769-$2,894 and $2,394, respectively.[5]

Setting and Population

Drug Class for Review: Erythropoiesis-stimulating agents

Age Range: ≥1 month

Gender: Male & female

Approval Criteria

Approval Diagnoses

Condition	Submitted ICD-9 Diagnoses*	Inferred Drugs	History Date Range	Client Approval (initials)
(Epoetin & Darbepoetin)				
Anemia of chronic renal failure	585.xx-586.xx	N/A	1 year	
Anemia with chemotherapy for Non-myeloid cancer	140.xx – 239.xx (excluding 205.xx [myeloid leukemia])	--	1 year	
	--	Antineoplastics	90 days	
Anemia with zidovudine-treated HIV	042.xx, 795.71, 079.53, V08	--	90 days	
	--	Zidovudine	30 days	
Elective surgery**	Non-cardiac, nonvascular	--	--	
Allogenic blood transfusion in surgery patients	Non-cardiac, nonvascular	--	--	

*Please refer to Appendix A **Call center (no ICD-9 codes submitted yet due to future date for surgery)

Denial Criteria

- Darbepoetin use in patients < 18 years of age (not studied in pediatric patients)
- Absence of approval diagnoses or procedure codes
- Use in patients with uncontrolled hypertension or other contraindications
- Patients not responding to usual doses of therapy; prescriber to rule out causes for delayed / diminished response before continuing therapy, including:
    - Iron deficiency
    - Underlying infectious, inflammatory, or malignant processes
    - Occult blood loss
    - Underlying hematologic diseases
    - Folic acid or vitamin B12 deficiency
    - Hemolysis
    - Aluminum intoxication
    - Osteitis fibrosa cystica

*** Please refer to Appendix B

Required Documentation

Laboratory results:	X	Progress notes:	
MedWatch form:			

Disposition of Edit

- **Denial:** Edit 682 “Clinical Edit”

Approval Period

1 Year

References

1. Ortho Biotech Products, L.P. http://www.procrit.com/profonly/pdf/Procrit_PI.pdf. Accessed 6/25/02.
2. Amgen Inc. http://www.renaladvances.com/resources/products/epogenpi.html. Accessed 6/25/02.
3. Wilber RL. Detection of DNA-recombinant human epoetin-alpha as a pharmacological ergogenic aid. Sports Med 2002;32(2):125-42.
4. Amgen Inc. http://www.aranesp.com/prescribing_info.html. Accessed 6/25/02.
5. The Medical Letter, Inc. Darbepoetin (Aranesp) – A long-acting erythropoietin. Med Letter 2001;43(1120):109-110.

Appendix A

ICD-9 Diagnosis Code Definitions	
Condition	**Codes**
Non-myeloid cancer	140.xx – 239.xx (excluding 205.xx [myeloid leukemia])
Chronic renal failure	585.xx-586.xx
HIV	042.xx, 795.71, 079.53, V08

Appendix B

Lab Values Required to Initiate and Monitor Therapy
Transferrin sat ≥ 20% is required to assure adequate iron stores to support erythropoiesis
Ferritin ≥ 100ng/ml is required to assure adequate iron stores to support erythropoiesis
HCT < 30% for chronic renal failure patients not receiving dialysis (initial therapy)
Endogenous serum erythropoietin < 500 mUnits/ml for HIV patients (higher levels unlikely to respond to therapy
Lab Values That Contraindicate Epoetin/Darbepoetin Therapy
HCT> 36% or Hgb > 12 g/dl in patients receiving continuing therapy (risk of adverse events)